A Dissertation on

CORRELATION OF BODE INDEX WITH THE PRESENCE OR ABSENCE OF PULMONARY HYPERTENSION TO PREDICT FURTHER ADMISSIONS IN COPD

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CERTIFICATE

This is to certify that this dissertation entitled "**CORRELATION OF BODE INDEX WITH THE PRESENCE OR ABSENCE OF PULMONARY HYPERTENSION TO PREDICT FURTHER ADMISSIONS AMONG PATIENTS WITH COPD**" submitted by **Dr.ANIRUDH. J. SHETTY** to the Tamil Nadu Dr.MGR Medical University is in partial fulfillment of the requirement of the award of M.D. DEGREE (BRANCH -1) and is a bonafide research work carried out by him under direct supervision and guidance.

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DECLARATION

I solemnly declare that the dissertation entitled **"CORRELATION OF BODE INDEX WITH THE PRESENCE OR ABSENCE OF PULMONARY HYPERTENSION TO PREDICT FURTHER ADMISSIONS AMONG PATIENTS WITH COPD"** was done by me at the Government Stanley Medical College and Hospital during 2009-2011 under the guidance and supervision of PROF. Dr. MADHAVAN M.D. The dissertation is submitted to the Tamilnadu Dr.MGR Medical University towards the partial fulfillment of requirements for the award of M.D.DEGREE (BRANCH – I) in general medicine.

Place :

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CONTENTS

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD), is a devastating lung disease which leads to progressive difficulty in breathing. COPD prevelance and mortality are continuing to increase despite adequate measures due to continued exposure to risk factors especially smoking among women and adolescents. GOLD estimates suggest that COPD will rise from sixth to third most common cause of death by 2020.The cost on health resources is immense.

COPD (Chronic Obstructive Pulmonary Disease) is an umbrella term used to describe lung disease associated with airflow obstruction which is not reversible. Mostly, emphysema and chronic bronchitis, either alone or combined, come in this category. There is a debate whether this term also includes asthma. However, as a general rule, it is not included. Although it does have obstructive components, it is reversible and is considered a restrictive lung disease. Many patients with COPD also have an asthmatic component to their illness as well.

Usually the severity of COPD is graded based on only Forced Expiratory Volume (FEV1). As COPD is a multisystem disorder FEV1 alone cannot determine the outcome in these patients. Hence a multidimensional grading system was designed which included four variables body-mass index (B), the degree of airflow obstruction (O) and dyspnea (D), and exercise capacity (E) measured by the six-minute–walk test.

AIMS AND OBJECTIVES

1. To correlate severity of BODE index to severity of Pulmonary Hypertension.
2. To predict future respiratory admissions based on the disease severity as assesed by BODE index and Pulmonary Hypertension.
3. By initiating appropiate and adequate therapy along with cardiopulmonary rehabilitation measures whether the severity of BODE index can be downsized.

REVIEW OF LITERATURE COPD

DEFINITION

Chronic obstructive pulmonary disease (COPD) has been defined by the Global Initiative for Chronic Obstructive Lung Disease(GOLD)[1],an international collaborative effort to improve awareness ,diagnosis and treatment of COPD ,as a disease state characterized by airflow limitation that is not fully reversible .

COPD includes emphysema ,an anatomically defined condition characterized by destruction and enlargement of lung alveoli;chronic bronchitis ,a clinical condition with chronic cough and phlegm; and small airways disease ,a condition in which small bronchioles are narrowed .COPD is present only if chronic airflow obstruction occurs; chronic bronchitis without chronic airflow obstruction is not included within COPD.

Chronic bronchitis is clinically defined as chronic productive cough for three consecutive months in two consecutive years.

Emphysema, pathologically defined 'as an abnormal enlargement of the air spaces distal to the terminal bronchioles accompanied by destruction of their walls and with absence of fibrosis'.[2]

COPD, though considered a chronic, debilitating disease, can be slowed down if given appropriate management. Bronchodialators , mucolytics, nasal oxygen and cardiopulmonary rehabilitation go a long way in slowing the progression

EPIDEMIOLOGY

At least 10 percent of the world's population over 40 years of age may have chronic obstructive pulmonary disease (COPD), according to new data [3]. The new statistics, suggest that the chronic lung disease is 3 times more common than previous estimates [4, 5, 6, 7].

The World Health Organization (WHO) estimates that COPD kills more than 2.75 million people each year. Worldwide it ranks as the fourth leading cause of death, alongside HIV/AIDS [7]. ."COPD is like an iceberg: The burden of disease that is the tip of the problem. COPD is rapidly increasing in prevalence, but also many people are unaware of the disease that they have .

Effective treatments exist that can improve the lives of people with COPD and can slow the progression of the disease, but patients can only receive the benefits of these therapies if we stop ignoring COPD and increase our awareness.

Most national statistics on COPD have been based on the proportion of the population that is being treated for COPD. The disease however, remains undiagnosed until it is already quite advanced so this method is likely to underestimate the proportion of the population that ***has*** COPD.

In 2010, almost 24 million adults over the age of 40 in India had COPD. It is expected that this number to increase 34% to approximately 32 million by 2020. The most obvious explanation for this is that COPD is predominately a disease of men and only 40% of cases in India occur in women. The strong association between age and COPD means that the prevalence of COPD in the future will be especially sensitive to the increased survival that will result as access to healthcare increases; even though the disease is irreversible, its progress can be significantly slowed by quitting smoking and seeking medical care. Fewer than half of the estimated 23.68 million prevalent cases in 2010 were in the population between the ages of 40 and 60 years (8.25 million), which indicates that chronic obstructive pulmonary disease (COPD) is a disease of the aged in India. The number of men with COPD in 2010 (approximately 14.11 million) was one and a half times the number of women with COPD in 2010 (approximately 9.57 million);

the most obvious explanation for this is the higher smoking rates in men than women in India.

The prevalence of COPD reported in different population based studies from India is highly variable[7]. According to some studies, in male subjects prevalence rate is about 2.12% to 9.4% from North India and 1.4% to 4.08% from South India. The respective ranges for female subjects vary from 1.33% to 4.9% in the North and from 2.55% to 2.7% in South India. For rounded-off median prevalence rates were assessed as 5 percent for male and 2.7 percent for female subjects of over 30 years of age[7]. The disease is distinctly more common in males.

The prevalence was found to increase with increasing age, especially in the males,in those with more than 20 pack–yrs of smoking and in low income subjects. The male to female ratio had varied from 1.32:1 to 2.6:1 in different studies with a median ratio of 1.6:1[(11).]

RISK FACTORS

1. Tobacco smoke

Tobacco smoke, some say contains more than 4000 chemical constituents, is the most important cause. Both cigarette and 'bidi'

smoking are equally dangerous.[8] Various other forms of smoking like pipe smoking and hookah are also important in causing COPD. There is no reliable information on smoking associated COPD in women in whom the overall prevalence of smoking is very low. Besides active tobacco smoking, exposure to smoking from others i.e. passive smoking, better termed as Environmental Tobacco Smoke (ETS) exposure, may also play a contributory role especially in nonsmoker individuals in women.(9,10)

INDOOR AND OUTDOOR POLLUTION

Certain solid fuels such as dried dung, wood and crop residue used for cooking and heating is an important cause of pollution of the indoor air. It is responsible for a large number of COPD patients especially women in particular.[11-14]

Exhausts from vehicles and industrial units; dusts, fumes and smoke from burning of crop residues in the field constitute important sources of air pollution. Chronic exposure to polluted air is an important cause of chronic respiratory diseases such as the COPD.[15-18]

GENETIC RISK FACTORS:

Homozygosity for the Z allele of the alpha1-antitrypsin gene is the only established risk factor. Heterozygotes for the Z allele may also be at risk. Mutations involving the structure of alpha1-antitrypsin or the regulation of gene expression have been identified as risk factors. Alpha1-antichymotrypsin, alpha2-macroglobulin, vitamin D-binding protein and blood group antigens, have been associated with the development of COPD.

OTHER RISK FACTORS :

1. GENDER: Some studies show that the prevelance of disease in developed countries is almost equal[18].But many studies have proven that females are susceptible to tobacco than males[19-21]
2. RESPIRATORY INFECTIONS during childhood
3. LOW SOCIOECONOMIC STATUS
4. CO MORBIDITIES

SYMPTOMS:

Typically, after smoking 20 or more cigarettes a day for more than twenty years, patients with COPD come to the hospital.

1. Symptoms due to emphysema

   Patients affected predominantly by **emphysema**, shortness of breath may be the major symptom. Dyspnea usually is most noticeable during increased physical activity, but as emphysema progresses, dyspnea occurs at rest.

2. Symptoms due to chronic bronchitis

   Chronic cough with sputum is the main symptom. The sputum is usually clear and thick.Recurrent respiratory tract infection is very common which can cause fever, dyspnea, production of purulent (cloudy and discolored) sputum and wheezing. Infections occur more frequently as bronchitis progresses.

3. Symptoms due to advanced COPD symptoms

   - cyanosis may develop
   - Headaches, clouding of consciousness, altered behaviour due to retention of carbon dioxide in blood.

- Weight loss occurs because it is a chronic inflammatory state and there is additional energy that is required to breathe.
- In advanced COPD, there is destruction of gas-exchanging air spaces in the lungs and this blocks the flow of blood through the lungs. As a result, the pressure in the pulmonary artery increases resulting in pulmonary hypertension. This results in development of right heart failure also known as Cor pulmonale .
- Patients with COPD may cough up blood (hemoptysis). Usually hemoptysis is due to damage to the inner lining of airway blood vessels;

PATHOPHYSIOLOGY OF COPD

Neergard and Wirz in 1927was the first to show expiratory airway resistance. Some studies from corbin showed increased static lung volumes (RV, FRC, and TLC), in people who were chronic smokers.

COPD pathophysiology is not completely understood. Major role is that of chronic inflammation of the cells which line the bronchial tree. Smoking, and other airway irritants, increases the ongoing inflammatory response which leads to hyperactivity of the airways, whereby the smooth muscle of the airways constrict and narrow excessively. Airways become swollen, excess mucus is produced and the cilia to function poorly which leads to pooling of the airways with mucus.

As excess mucus is produced, it begins to pool in the airways, providing a breeding ground for bacteria to multiply. This leads to further inflammation, in the bronchial tree and bacterial infections which occur frequently in COPD patient.

A new hypothesis for the beginning of COPD, that the immune response to inhaled agents, mainly cigarette smoke, is directed toward

the epithelium of airway, due to oxidative DNA damage of the lung epithelial barrier cells (LEBCs).

The steps of this model are as follows.

1) Cigarette smoke causing oxidative DNA damage to LEBC.

2) The acquired mutations of Lung epithelial barrier cells (LEBCs) are expressed at the microsatellite DNA level.

3) Dendritic cells (DCs) recognize the altered LEBCs as “foriegn”. Dendritic cells travel to the lymph nodes,and then it presents it to the naïve T-lymphocytes.

4) There is a predominant CD8+ cytotoxic T-lymphocyte proliferation. The CD8+ cells, release perforin and granzymes, which attack the altered LEBCs activating cell death cascade.

STUDIES SUPPORTING THIS HYPOTHESIS

Oxidative DNA damage of LEBCs in COPD

There are number of different defense mechanisms against noxious or infectious agents in the respiratory tract. In the airways, the first line of defence the constitutes the LEBCs and have been shown to differ in number and function in smoke-related diseases such as

COPD [23–25]. Oxidative stress is believed to be a central component in COPD pathogenesis as smokers are exposed to thousands of radicals and reactive chemicals with every cigarette,. ROS, reactive nitrogen species (RNS) and carbon-centred radicals are the major constituents of smoke . Also endogenous sources of ROS, such as those produced by activated alveolar macrophages and neutrophils in response to smoke, cause further epithelial cell damage . Increased ROS production is linked to oxidation of proteins and DNA which may cause direct lung injury or induce a variety of cellular responses. ROS can cause damage to nucleic acids, resulting in base modifications, strand breaks, mismatches and cross-links, leading to increased levels of somatic mutation . These mutations are supposed to be corrected by endogenous repair processes, such as the human DNA MMR system. However, post-translational inactivation of repair enzymes by free radicals may cause the accumulation of damaged DNA .

The oxidative burden of smoking damages the DNA of lung epithelial barrier cells (LEBCs) and inactivates the human DNA mismatch repair system, leading to acquired somatic mutations of LEBCs. Altered LEBCs are recognised as ‘‘nonself’’by the host,

inducing an abnormal immune response towards the altered LEBCs, resulting in the activation of cell death cascades.

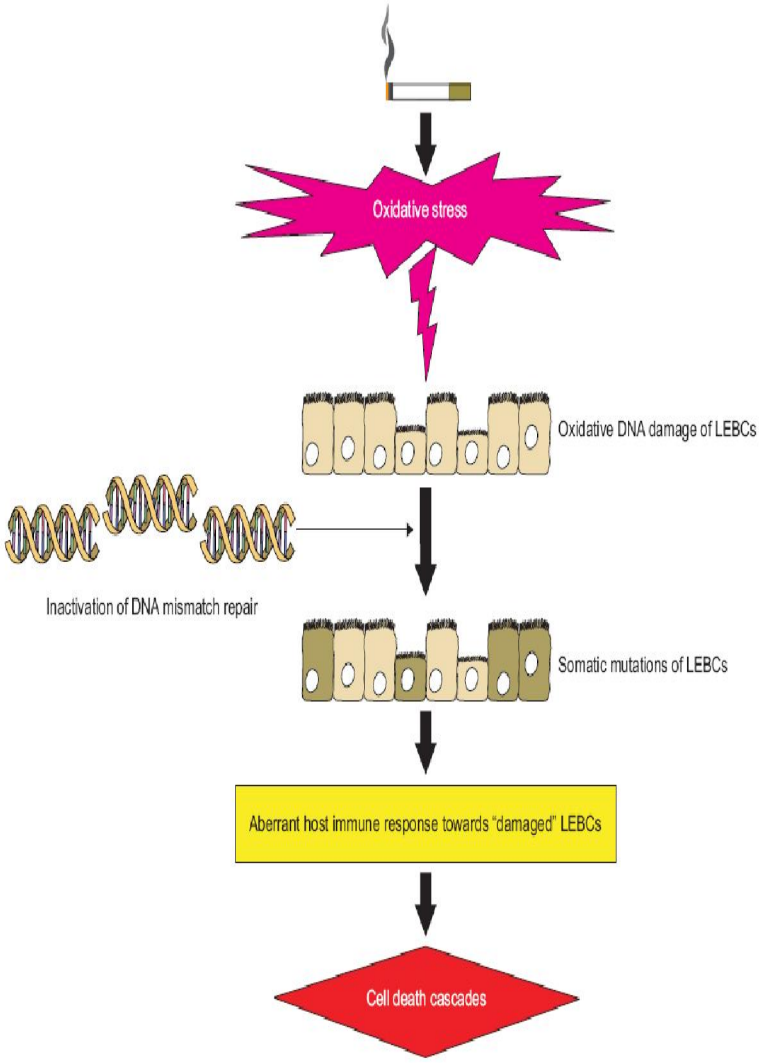


Figure 1. The proposed model for the beginning of COPD. Cigarette smoke causing oxidative DNA damage to LEBC and inactivates the human DNA mismatch repair system, leading to acquired somatic mutations of LEBCs. Altered LEBCs are recognized as "foreign" by the host, inducing an abnormal immune response towards the altered LEBCs. This results in the activation of cell death cascades.

Interestingly, female smokers have accelerated metabolism of cigarette smoke leading to increased burden of DNA adducts [25, 26] and hence are more susceptible to somatic mutations, which may predispose to COPD [25, 26.]

Acquired somatic mutations of LEBCs

Molecular damage in the lung epithelium is present even after smoking cessation. Microsatellite DNA instability has been found in sputum cells of COPD patients28. Studies have shown microsatellite instability exclusively in the sputum epithelial cell subpopulation [28], isolated by immunomagnetic separation.

The MMR system is a DNA repair mechanism known to be very effective at identifying and subsequently rectifying errors in DNA replication. The MMR corrects base substitutions and frameshift errors. It has been demonstrated that oxidative stress associated with cigarette smoke and chronic inflammation might damage protein components of the MMR system, leading to its functional inactivation [28], . Moreover, Makris *et al.* [29] showed a significant association between microsatellite DNA instability and COPD exacerbations, indicating a link between altered DNA MMR system and oxidative DNA damage due to frequent COPD exacerbations or *vice versa* [29].

Host immune response to the altered LEBCs:

There are many types of cell damage which leads to DNA fragmentation and destruction of the repair potential that allow its recognition as "foreign" [30, 31].,

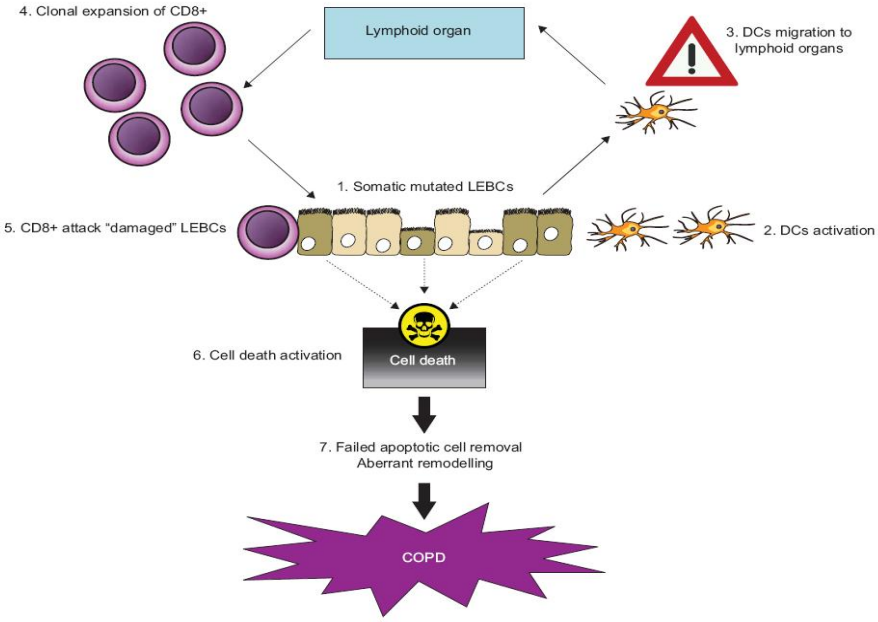


Figure 2. Acquired somatic mutations of lung epithelial barrier cells (LEBCs) in chronic obstructive pulmonary disease (COPD).

In this theory it is thought that once the LEBCs suffer oxidative DNA damage they are detected as "nonself" by the Dendritic Cells [32].

After sampling of antigen in the periphery, DCs migrate to regional lymph nodes, where they activate naïve T-cells [33].Studies show that it is highly likely that DCs are implicated in the pathogenesis of

COPD, not only in the initiation but also in the perpetuation of chronic airway inflammation [34, 35, 36]. DCs interact with naïve lymphocytes to induce one of three predominant responses: T-helper cell (Th) type 1, Th2 or T-regulatory [37.]

INDUCTION OF A PREDOMINANTLY CD8+ CYTOTOXIC TYPE I T- LYMPHOCYTE PROLIFERATION:

It has been proven that, in COPD, DCs help in the induction of a predominantly CD8+ cytotoxic type I T-lymphocyte response [38, 39], . This causes chronic airway inflammation with increased numbers of CD8+ cells and release of IFN inducible protein 10, IFN-γ and tumour necrosis factor (TNF)-α, as well as perforin and granzymes [40, 39, .]

CD8+ cells attack the altered LEBCs and perform cytotoxic functions, activating cell death cascades[41, 42, 43]. In agreement with this, Chrysofakis *et al.* [43]showed that CD8+ T-cells from patients with COPD produced more perforin and were extremely cytotoxic. Perforin-dependent events leads to apoptosis.Apoptosis, is anti-inflammatory in nature, but if the apoptotic bodies are not removed in time leads to persistent inflammation .

MMP-12 in Smoking-Related COPD

Cigarette smoking is the major risk factor for both chronic bronchitis and emphysema. .[46]Inflammation, proteinase imbalance, oxidative stress, all appear to be involved in the pathogenesis of COPD and the matrix metalloproteinase 12 (MMP-12) plays a role in every of these processes (Figure 3).

Usually there is an innate balance in the body between the protective factors like protease inhibitors , elastase inhibitors and harmful factors like proteases ,elastases ; when the normal milieu of this balance is disrupted by external factors which may include infection , undue inflammatory stimulation then there will continuous damage to the viscera ; Chronic obstructive pulmonary disease can be explained in part by this mechanism too [47] ;This protease-antiprotease imbalance is now assumed be due to inflammation which is chronic .[47]Macrophage elastase MMP-12 (inhibited by TIMP-1) and neutrophil elastase (inhibited by alpha-1-antitrypsin) are the most common elastases found in the lung. TNF alpha, is the major recruiter of neutrophils to the lung that is released from the cell membrane by MMP-12, ; IFN-gamma also recruits neutrophils and stimulates MMP-12 activity.[47,48,49]

One more molecule which also recruits neutrophils and stimulates MMP-12 activity is IFN Gamma.[47,48,49] These neutrophil

elastases and oxidants secreted in the environment with inflammation mediate much of the destruction of lung tissue.[50]Elastin fragments itself are chemotactic, which recruits monocytes. Some of these differentiates to form alveolar macrophages that is composed of bulk of the inflammatory cells accumulating in the alveolar airspaces and interstitium in emphysema.[51]

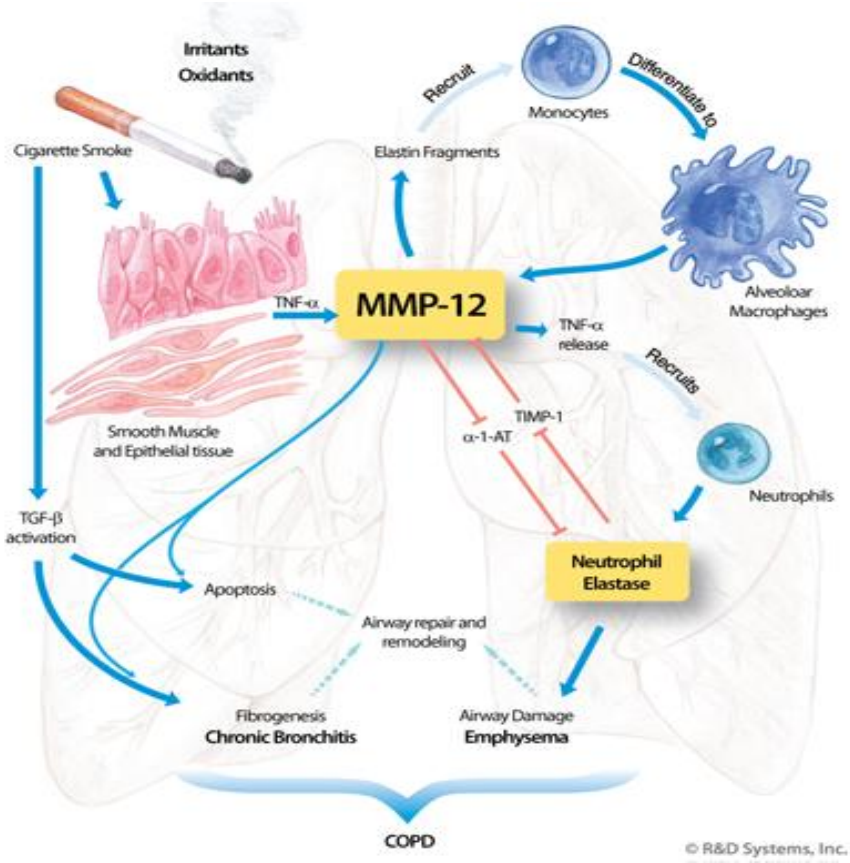


Figure 3. MMP-12 is produced by alveolar macrophages, smooth muscle cells, and epithelia in response to cigarette smoke. It is a key molecule in the recruitment of inflammatory cells, release of TNF-alpha, and pathways downstream of TGF-beta activation. These activities lead to the airway damage, fibrogenesis, repair, and remodeling that are the hallmarks of COPD.

One more important thing supporting this hypothesis is the fact that increased levels of MMP-12 is seen in sputum of patients with COPD. Also some experiments in mouse have shown that MMP-12 deletion stops the development of smoking induced COPD. Several other studies have shown that neutrophil elastase inhibition significantly reduces lung damage. Hence deficiency of human alpha-1-antitrypsin, which is a inhibitor of human neutrophil elastase, leads to susceptibility to COPD.

TREATMENT OF COPD

The first important thing in treating chronic obstructive pulmonary disease is to understand the reality that this is a disease which cannot be cured but can only be kept under control if appropriate lifestyle changes and adherence to both the medication and health advice is strictly followed ;

The main aim in treatment of COPD include:

- slowing the decline in lung function;
- relieving symptoms, such as dyspnea and cough;
- decreasing exacerbations
- improving quality of life

SMOKING CESSATION

Among the many factors which add to the damage inflicted by COPD, the prime one is smoking ; putting an end to this health hazaerd goes a long way in curtailing the morbidity and mortality of COPD ; `

The most important step is encouraging smoking cessation. Smoking is directly related to loss of lung function . Even in advanced disease patient can benefit from smoking cessation. It also stops the loss of lung function in younger patients with relatively mild disease.

This may be aided by the use of nicotine replacement therapy (by gum,transdermal patch or inhaler) or bupropion ,a noradrenergic antidepressant. Bupropion has been shown to be quite effective in this regard .

TREATMENT OF RESPIRATORY INFECTIONS

Purulent sputum is treated with oral tetracycline or ampicillin 250 mg 6 hours or cotrimoxazole 960 mg 12 hourly for 10 days.

In the absence of response, a sputum culture and sensitivity is done and the antibiotic changed accordingly.

BRONCHODILATOR THERAPY AND STEROID THERAPY

BETA $_2$ ADRENORECEPTOR ANTAGONISTS:

- Inhalation of beta$_2$- adrenoreceptor agonists like salbutamol 200 mcg or terbutaline 500 mcg 6 hourly,in mild to moderate disease.
- These agents are short-acting and needed to be taken frequently. Long –acting beta-stimulants(salmeterol and formoterol) are the preferred agents for achieving bronchodilation.
- These agents may reduce the incidence of infective exacerbations since these drugs reduce the adhesion of bacteria to airway epithelial cells.

ANTICHOLINERGICS:

Anticholinergic drugs, form one of the important part of the treatment schedule in decreasing the frequency and severity of COPD exacerbations. Some of the examples are ipratropium bromide, thiotropium bromide. They act by decreasing the secretion of mucus in response to the inflammatory onslaught and also significantly causes symptomatic improvement.

Despite these advantages, they seem to play not much of a role in the emergency room, as they seem to be of more benefit in modulating the disease course in the long run if used regularly.

CORTICOSTEROIDS:

Basically COPD is a inflammatory disease and it was widely believed that steroids would be the ultimate therapy . Despite the initial hope they generated steroids seem to play not much of a role in the management of COPD as compared to bronchial asthma.

Hence, inhaled corticosteroids are not indicated for the treatment of COPD. They have a limited role in patients with COPD. Only about 10 percent of patients with COPD show a significant improvement . The reason is that different mediators cause inflammation in asthma and COPD. Oral theophylline in seleced cases.

PULMONARY REHABILITATION

The various techniques of physical therapy (upper extremity exercises, controlled breathing techniques), targeting the training of respiratory muscles in patients with COPD.

Intermittent mechanical ventilation in stable COPD stages, to rest inspiratory muscles.

OXYGEN THERAPY

1. Controlled oxygen therapy,

   A flow of 2-4 liters / min is satisfactory, mask or nasal tube can be used (15 to 20 minutes, with intermission).

2. Long-term oxygen therapy has the benefit of the reversal of

   Pulmonary hypertension.

GOLD Spirometric Criteria for COPD Severity

I. Mild COPD	* FEV1/FVC < 0.7 * FEV1 > or = 80% predicted	At this stage, the patient is probably unaware that lung function is starting to decline
II. Moderate COPD	* FEV1/FVC < 0.7 * FEV1 50% to 79% predicted	Symptoms during this stage progress, with shortness of breath developing upon exertion.
III. Severe COPD	* FEV1/FVC < 0.7 * FEV1 30% to 49% predicted	Shortness of breath becomes worse at this stage and COPD exacerbations are common.
IV. Very Severe COPD	* FEV1/FVC < 0.7 * FEV1 < 30% predicted or FEV1 < 50% predicted with chronic respiratory failure	Quality of life at this stage is gravely impaired. COPD exacerbations can be life threatening.

LIMITATIONS OF THIS CLASSIFICATION

FEV1 is very important for diagnosis and assessing severity of the disease. FEV1 is a good marker of disease progression and mortality but FEV1 does not correlate well with the degree of dyspnea[44], and the change in FEV1 does not reflect the rate of decline in patients' health[45]. As COPD is a multisystem disorder FEV1 alone cannot determine the outcome in these patients.

Hence a multidimensional grading system was designed which included four variables body-mass index (B), the degree of airflow obstruction (O) and dyspnea (D), and exercise capacity (E) measured by the six-minute–walk test. Each of these correlates directly with the prognosis.

MATERIALS AND METHODS

INSTITUTIONAL ETHICS COMMITTEE APPROVAL

Obtained

STUDY DESIGN

- Place: Govt. Stanley Hospital
- Study Design: Observational Study

Period of study **:** April 2011 to June 2011 ;

SAMPLE SIZE

- Cases : 100

INCLUSION CRITERIA

- A FEV1 of less than 15% from the baseline value measured 2o minutes after the administration of salbutamol with significant symptoms.

EXCLUSION CRITERIA

- Comorbid conditions previously detected CCF or UA, Myocardial infarction within the preceeding 4 months.

- An inability to take the lung function test and six minute walk tests.
- Asthma defined as an increase in FEV1 of more than 15% above the baseline value or of 200ml after administration of bronchodialator.
- Patients with TB,Bronchiectasis or any other parenchymal lung disease.

STUDY METHODOLOGY

All the patients who attend medicine opd and chest clinic opd will be screened acoording to the inclusion exclusion criteria and those patients who satisfy the criteria and give consent will be enrolled. For each subject- smoking, personal , occupational histories were obtained. Height and weight were also measured during the examination. Weight was measured by a weighing machine.

Height was measured in “mm” with the stadometer. Body mass index (BMI) was calculated using the formula.

BMI = Weight in Kgs / (Height in Ms)2

After clinical examination they will be subjected to PFT using a spirometer. Spirometry is performed using a portable spirometer

(SpiroPro; Erich Jaeger GmbH; Hoechberg, Germany) according to the American Thoracic society.

Using a Spirometer patient is asked to inhale deeply, after all air has

been expelled. After this maneuver patient is asked to rapidly exhale so that all the air is exhausted from the lungs.Results of spirometry tests vary, but are based on predicted values of a standardized, healthy population. FEV1 and FVC was obtained . %FEV1 was obtained. An average of three readings were taken. A history of the dyspnea experienced by the patient was taken. MMRC(Modified medical research council) dyspnea scale was used to score the patients dyspnea.

MMRC dyspnea scale

Grade 0 – no dyspnea / only on severe exertion.

Grade 1 – dyspnea on hurrying / walking up a hill.

Grade 2 – walks slower than normal at level/ pause while walking on level ground.

Grade 3 – stops for breath after walking 100 yards/few mins on level ground.

Grade 4 – too breathless to leave the house/ dyspnea on dressing.

The best of two 6-min walk tests performed at least 30-min apart was used for scoring. On a level ground patient were asked to walk for maximum possible distance within a duration of 6 minutes. If rest was taken in between then periods of rest were also included in the 6 minutes test period **.**

The BODE index was calculated for each patient using the body mass index, the threshold value of FEV1, the distance walked in 6 min, and the score on the modified Medical Research Council (MMRC) dyspnea scale **.**Each variable is given a point . Each subject is given a BODE score out of 10.Using appropriate statistical tests correlation and the strength of correlation will be computed between the severity of BODE INDEX, Pulmonary hypertension , risk of readmission and whether bode index can be downsized by rehabilitation**.**

Pulmonary hypertension is graded by TRPG (transtricuspid pressure gradient)based on ECHO.

- MILD – 30 to 45mmHg
- MODERATE – 45 to 70mmHg
- SEVERE- MORE THAN 70 mmHg

Patients were asked to undergo regular cardiopulmonary rehabitilation. They were also advised to take regular bronchodialators. After 6 months patients BODE index was calculated again.The number of times patients were admitted was checked using their discharge summaries. ECHO was done again and the severity of pulmonary hypertension determined.

BODE INDEX

BODE score	**0**	**1**	**2**	**3**
FEV1	>/= 65 %	50 – 64%	36 – 49%	< /= 35%
6 min walk Test	>350 ms	250 – 349ms	150 – 249 ms	<149 ms
Dyspnea Scale	0 – 1	2	3	4
BMI	> 21 kg/m2	<21 kg/m2		

Mild COPD 0 – 2

Moderate COPD 3 – 5

Severe COPD >/= 6

STATISTICAL ANALYSIS

After catergorizing the variables statistical analysis was done in 100 patients. Baseline data was collected from patients without and with mild, moderate and severe COPD. Ages, FEV1, number of admissions, pulmonary hypertension, of all subjects were the parameters analyzed.

The significance of difference in means between two groups was analyzed using the one way ANOVA F-test and the significance of difference in proportions by the Chi square test. Statistical significance was taken when the p-value was less than 0.05.

Table 1: BASELINE PARAMETERS OF THE STUDY POPULATION

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	100	30.00	85.00	52.5800	10.19624
WT	100	44.00	70.00	53.4700	5.39070
HT	100	1.30	1.72	1.5212	.09753
BMI	100	16.90	31.80	23.1930	3.26224
RRATE	100	14.00	22.00	17.7000	2.43916
FEVIPER	100	22.00	66.00	50.0100	11.68915
SPO2	100	89.00	99.00	97.8300	2.14643
TRPG	100	18.00	76.00	38.4100	15.72561
BODEINDE	100	.00	9.00	4.2100	2.44245
PIBODE	100	.00	8.00	3.5100	2.12486
PIFEV1	100	15.00	66.00	48.3300	13.26502
PITRPG	100	18.00	79.00	40.0200	16.68301

The above table enumerates the various parameters of the study population and their statistical mean, minimum value maximum value with standard deviation

Table 2 : SEX AND AGE DISTRIBUTION

SEX	FREQUENCY	PERCENT
MALE	23	23.00
FEMALE	77	77.00
TOTAL	100	100.00

Table 2 (a) . AGE GROUP

AGE GROUP	FREQUENCY	PERCENTAGE
30 – 40	14	14.00
41 -50	34	34.00
51 – 60	33	33.00
61 – 70	16	16.00
> 70	3	3.00
TOTAL	100	100

AGE GROUP	FEMALE	MALE	PERCENT
30 – 40	17.4 (4)	13.0 (10)	14.00
41 -50	30.4 (7)	35.1 (27)	34.00
51 – 60	34.8 (8)	32.5 (25)	33.00
61 – 70	8.7 (2)	18.2 (14)	16.00
> 70	8.7 (2)	1.3 (1)	3.00
TOTAL	100	100	100

Out of the 100 patients 77 were males and 33 were females. In the age group of (30-40) there were 14% of patients,(40 – 50) there were 34% of patients ,(50-60) there were 33% of patients,(60-70) there were 16% of patients and more than 70 there were 3% of patients.COPD is more common in middle aged people even though it did not reach statistical significance.

Table 3 .BODE SCORE & SEVERITY OF PHT

PHT	NUMBER	MEAN	MIN	MAX.	ST.DEV.
ABSENT	43	2.0233	.00	4	0.83062
MILD	35	4.8000	2.00	8	1.41005
MOD.	16	7.120	5.00	9	1.4746
SEVERE	6	8.667	8.00	9	0.5164
TOTAL	100	4.2100	0.00	9	2.4424

$p < 0.001$ hs

Out of the 100 patients 43 did not have pulmonary hypertension and their mean bode score was 2.0233. 6 patients had severe pulmonary hypertension(Mean BODE SCORE 8.667) ; 16 had moderate PHT,(mean BODE SCORE 7.120)and 35 had mild PHT ; according to our study the association between severity of pulmonary hypertension and high BODE score was statistically significant as shown by the p value < .001.

Table 5: COPD Vs BODE INDEX

	No	Mean	Standard Deviation	Minimum	Maximum
MILD	37	1.729	0.508	0.00	2.00
MODERATE	37	4.297	0.845	3.00	5.00
SEVERE	26	7.615	1.022	6.00	9.00

As the degree of COPD increases the mean bode score increases. People with mild COPD had mean bode score of 1.72 and severe COPD had a mean bode score of 7.6154.This is statistically highly significant as (p < .001)

Table 6 : ADMISSION Vs BODE INDEX

ADMISSION	N	MEAN	STD. DEV	MIN	MAX
0.0	53	2.5283	1.6005	0.00	8
1.0	30	5.133	1.11658	2.00	8
2.0	8	7.3750	1.40789	5.00	9
3.0	9	8.2222	0.66667	7.00	9

In our study of the 30 patients who got admitted once had a mean BODE score of 5.133. 8 patients got admitted twice had a mean BODE score of 7.3750. 9 patients got admitted thrice had a mean bode score of 8.2222. This is statistically highly significant($p < .001$).Hence as the BODE index increases the number of readmissions are more.

Table 7 : DEGREE OF COPD vs NO OF ADMISSIONS

COPD	NUMBER OF ADMISSIONS				
	0.0	**1.0**	**2.0**	**3.0**	**TOTAL**
MILD	36	1	0	0	37
MODERATE	14	22	1	0	37
SEVERE	3	7	7	9	26
TOTAL	53	30	8	9	100

$p<0.001$

Out of the 100 , 37 patients had mild COPD . They were admitted only once in the course of our study ;among those who had severe COPD , i . e 26 of them , 9 were readmitted thrice , and 8 were admitted twice ; as the severity increased the number of readmissions increased as shown by the p value <0.001 which is a statistically significant

Table 8 : SEVERITY OF PHT & NUMBER OF ADMISSIONS

PHT	NUMBER OF ADMISSIONS				
	0.0	1.0	2.0	3.0	TOTAL
ABSENT	43	0	0	0	43
MILD	8	27	0	0	35
MODERATE	2	3	7	4	16
SEVERE	0	0	1	5	6

In our study out of the 35 patients with mild pulmonary hypertension 27 got admitted once.16 patients with moderate pulmonary hypertension 3 got admitted once,7 got admitted twice and 4 got admitted thrice.6 patients with severe pulmonary hypertension 1 got admitted once and the rest 5 three times.Statistically this was highly significant as the p value is< 0.001. As the pulmonary hypertension increased the rate of readmission also increased.

Table 9 : PRE AND POST INTERVENTION STATISTICS ;

VARIABLE	N	MEAN	STD.DEVIATION	STD.ERROR MEAN
FEV1	100	50.0100	11.68915	1.16892
BODE	100	4.2100	2.44245	.24424
TRPG	100	38.4100	15.72561	1.57256

Table 10 .POST INTERVENTION PARAMETERS

VARIABLE	N	MEAN	STD.DEVIATION	STD.ERROR MEAN
P.I FEV1	100	48.300	13.2652	1.32650
P.I BODE	100	3.5100	2.12482	.21249
P.I TRPG	100	40.0200	16.6830	1.66830

Table 11 . PAIRED SAMPLE TEST

	PAIRED DIFFRENCE		T	p
	MEAN	STD.DEV		
FEV1 – PIFV1	1.6800	2.0259	7.616	<0.001
BODEINDE – PIBODE	0.7000	0.62765	11.153	<0.001
TRPG - PITRPG	-1.6100	1.91166	-8.422	<0.001

In our study we found out that the mean Bode reduced from 4.2 to 3.51 following intervention. But the mean TRPG continued to increase despite interventions

Chart 1

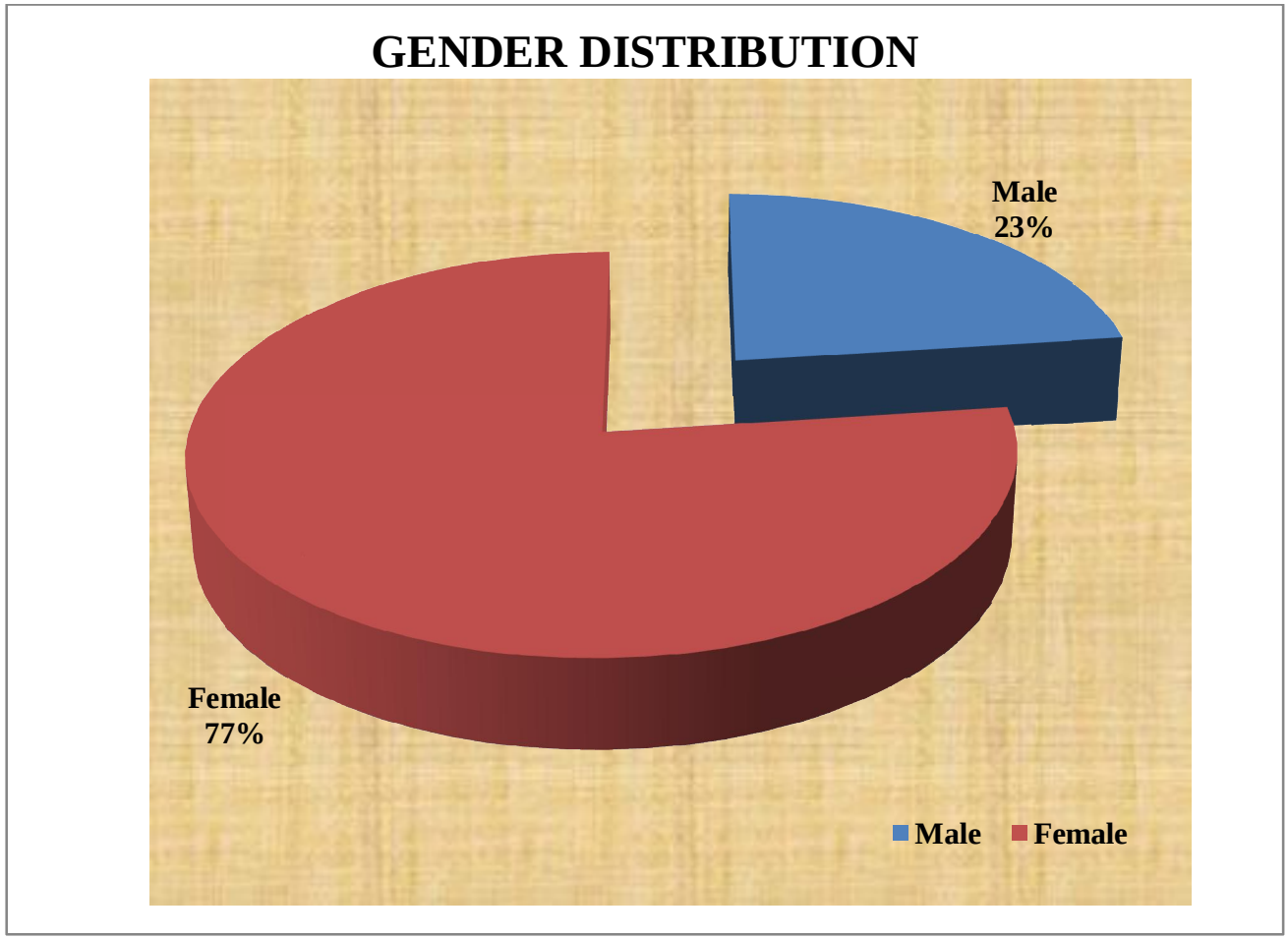


Chart 2

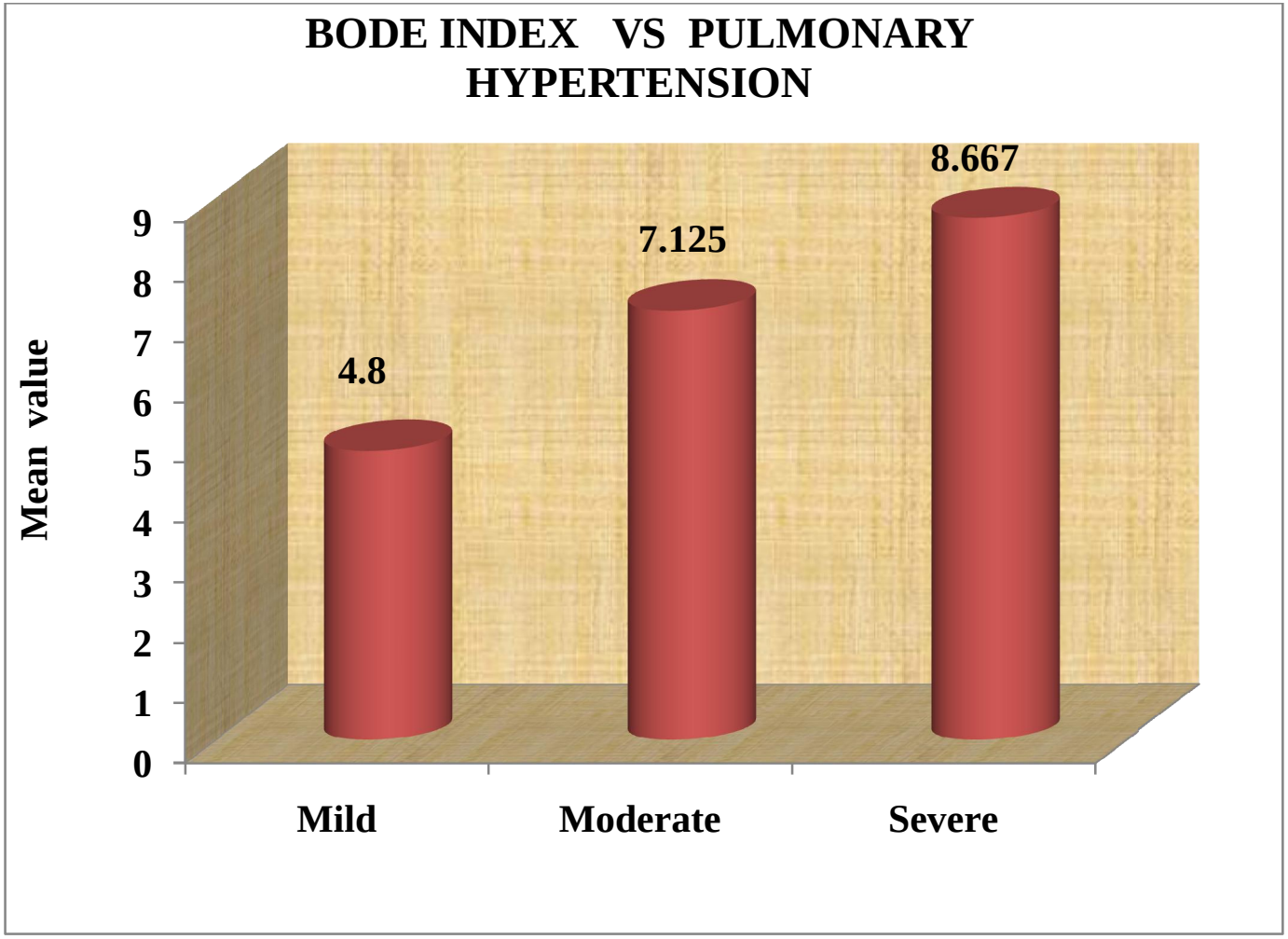

BODE INDEX VS PULMONARY HYPERTENSION
Mean value
0
1
2
3
4
5
6
7
8
9
4.8
7.125
8.667
Mild
Moderate
Severe

Chart 3

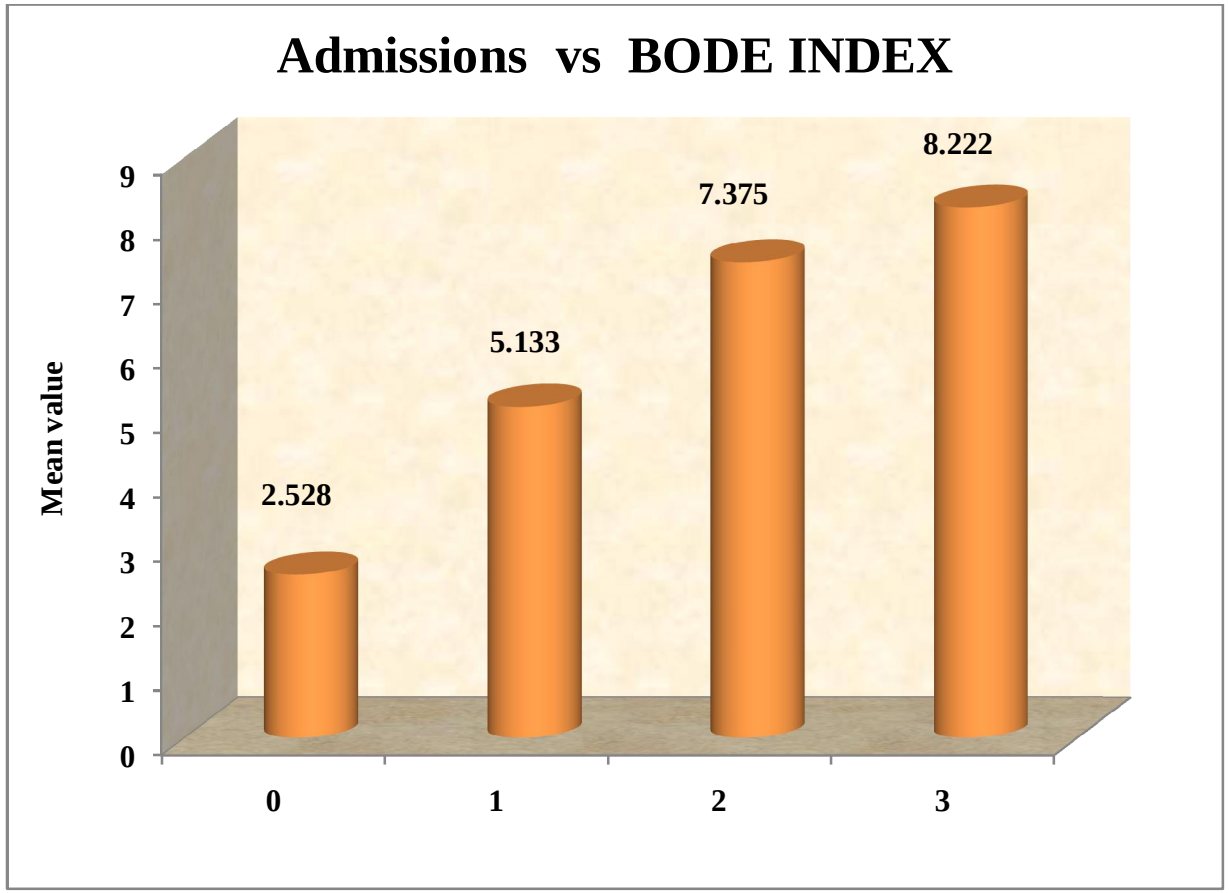

Admissions vs BODE INDEX
Mean value
9
8
7
6
5
4
3
2
1
0
2.528
5.133
7.375
8.222
0
1
2
3

Chart 4

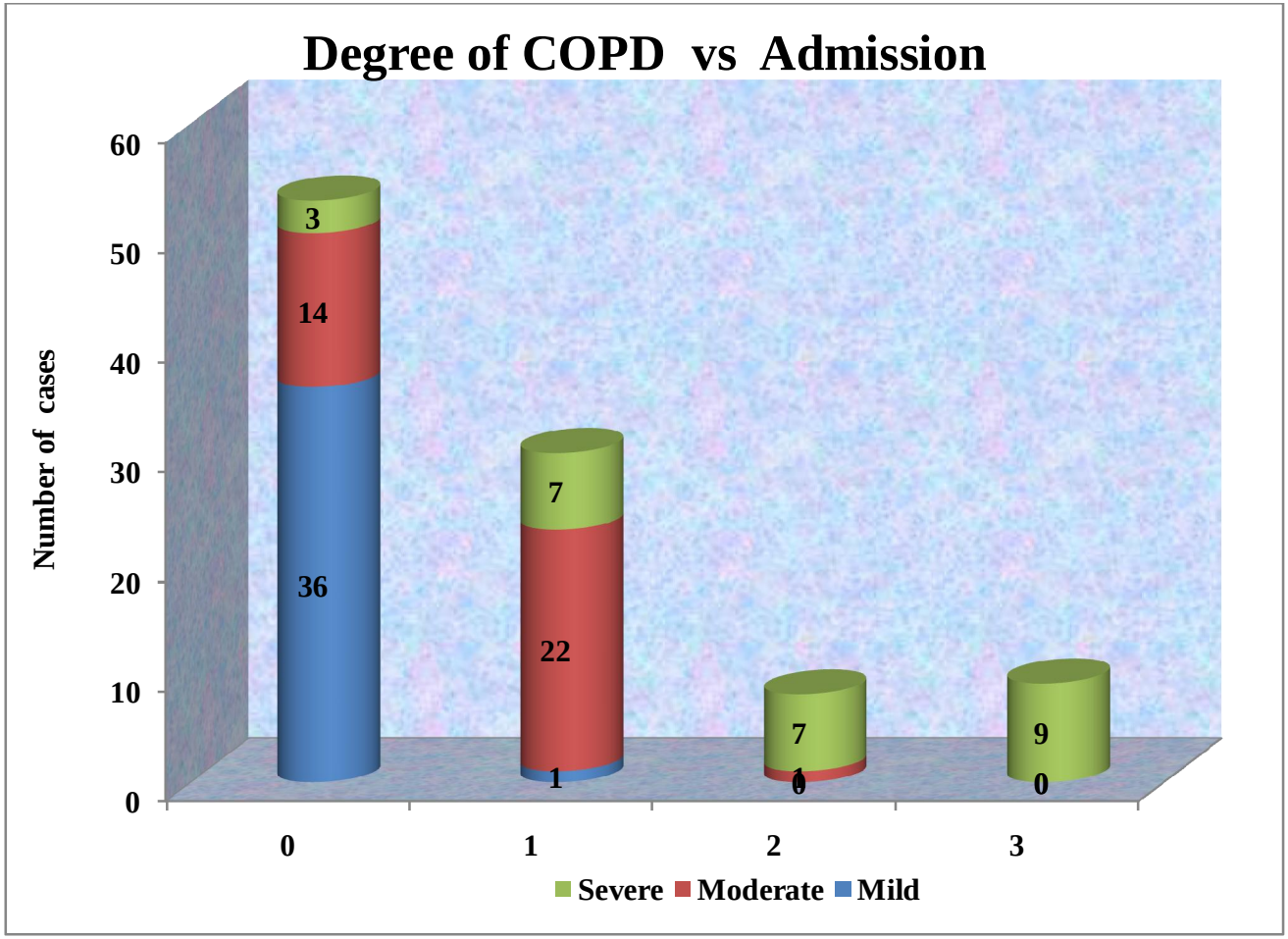

Degree of COPD vs Admission
Number of cases
60
50
40
30
20
10
0
3
14
36
7
22
1
7
0
9
0
0
1
2
3
Severe
Moderate
Mild

Chart 5

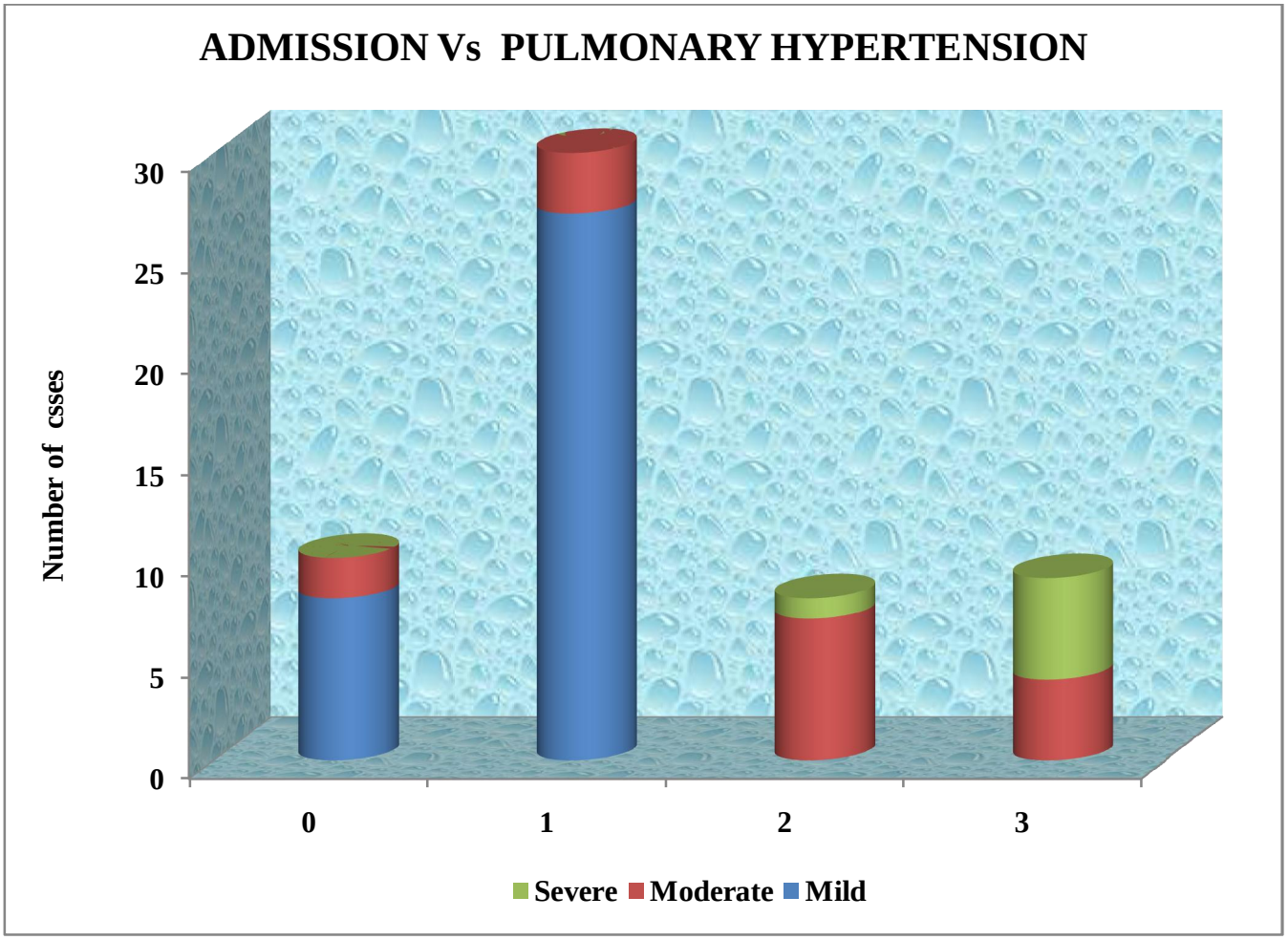

ADMISSION Vs PULMONARY HYPERTENSION
Number of csses
30
25
20
15
10
5
0
0
1
2
3
Severe
Moderate
Mild

Chart 6

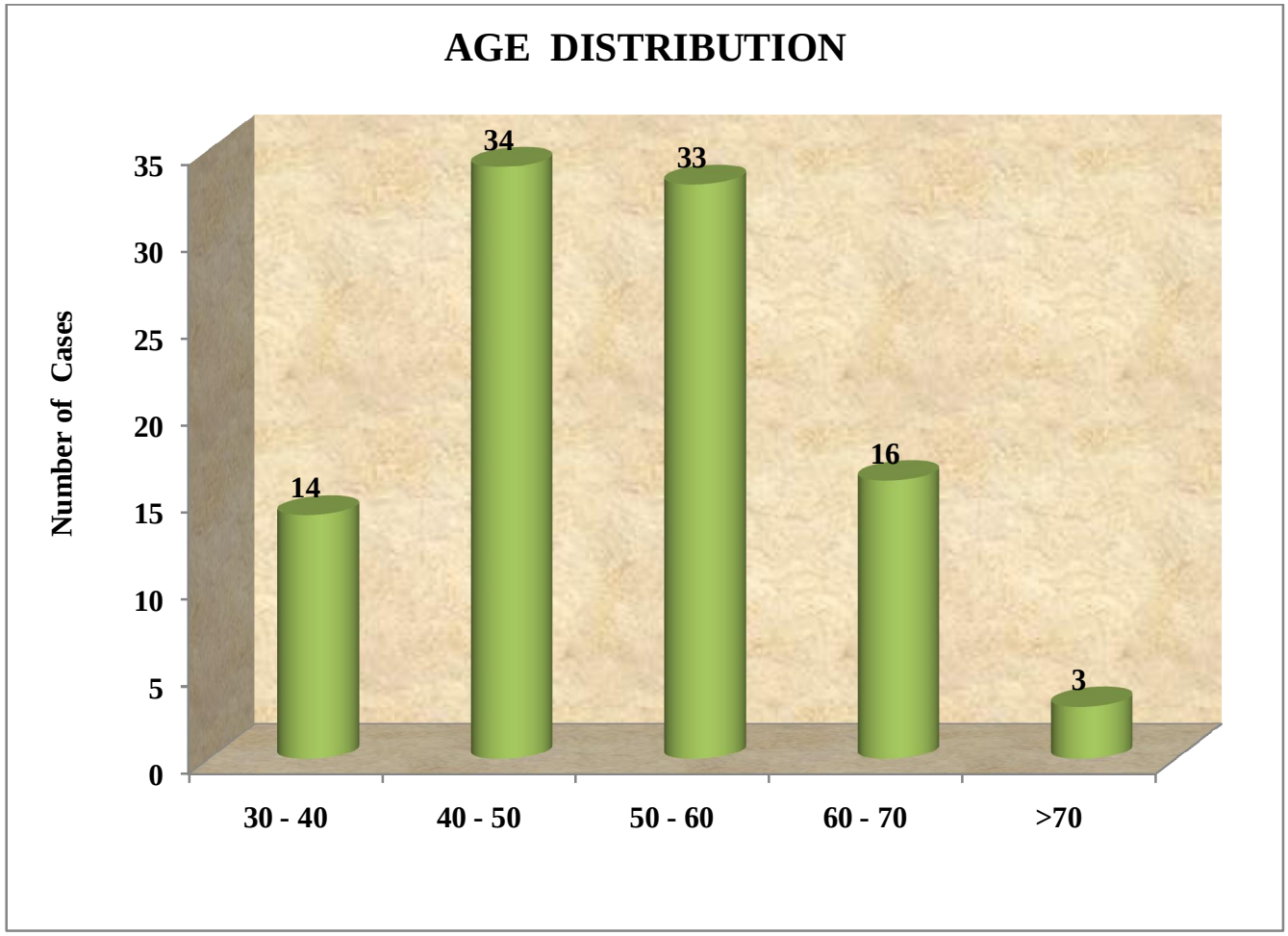

AGE DISTRIBUTION
Number of Cases
35
30
25
20
15
10
5
0
14
34
33
16
3
30 - 40
40 - 50
50 - 60
60 - 70
>70

Chart 7

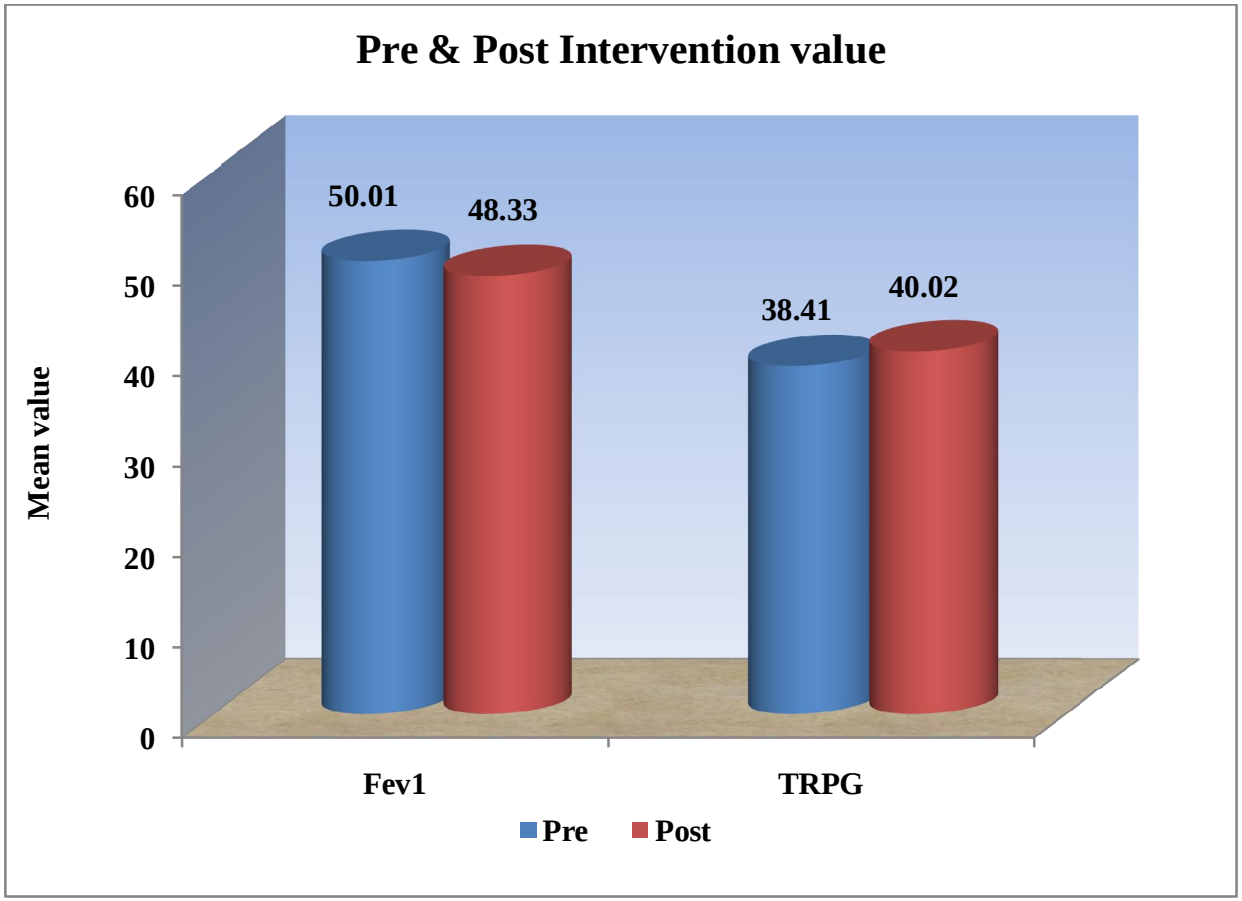

Pre & Post Intervention value
Mean value
60
50
40
30
20
10
0
50.01
48.33
38.41
40.02
Fev1
TRPG
Pre
Post

Chart 8

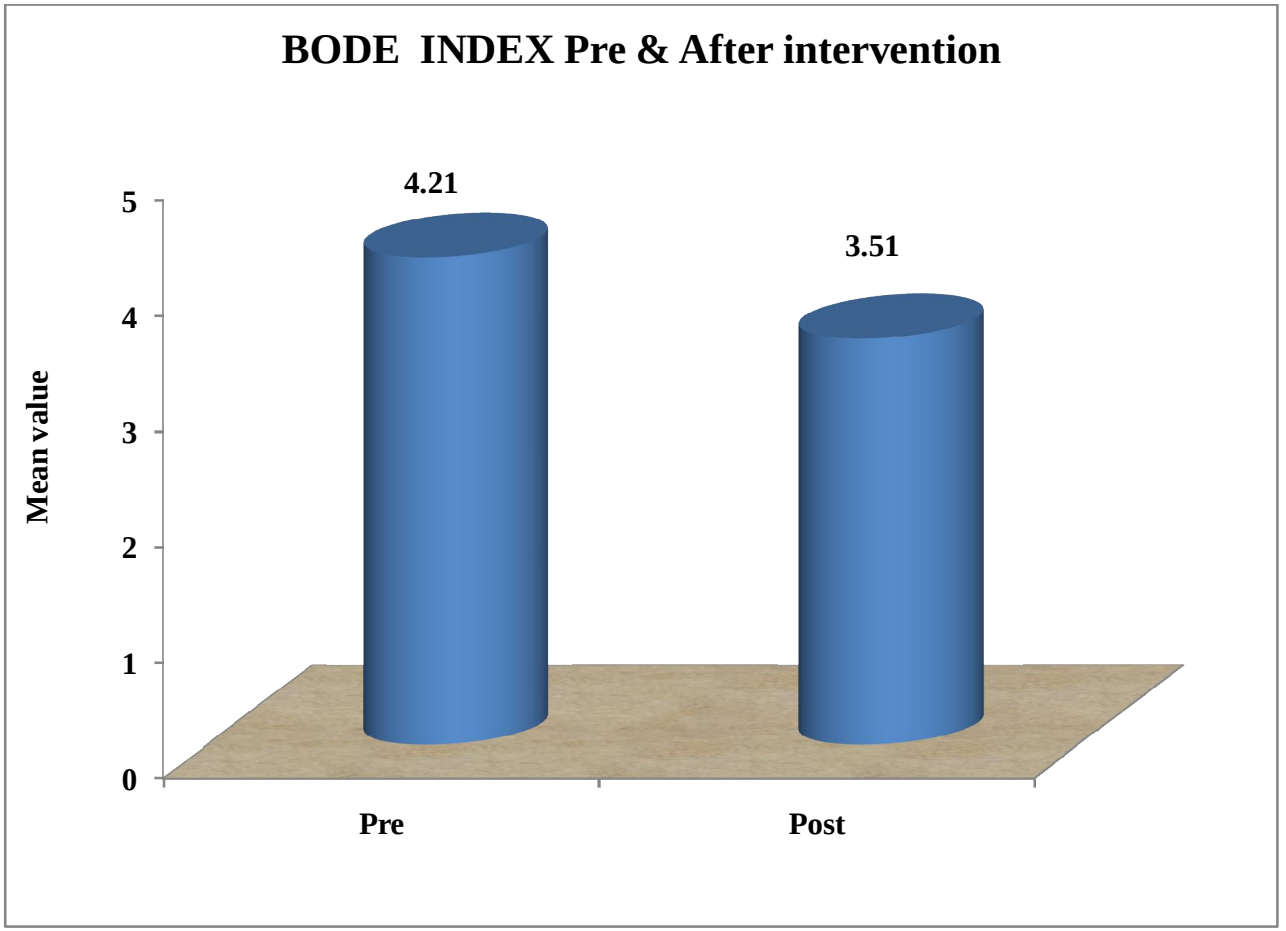
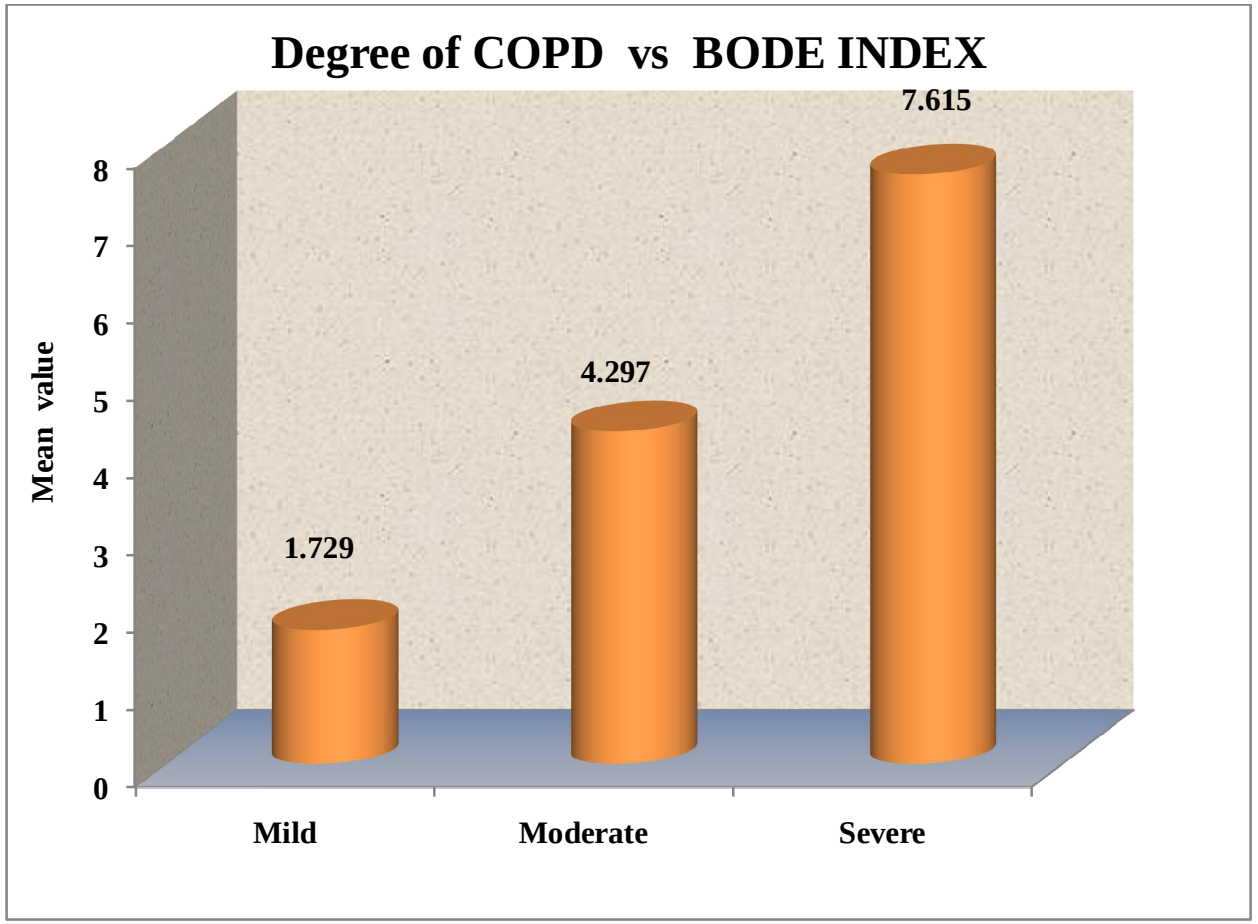

BODE INDEX Pre & After intervention
Mean value
5
4
3
2
1
0
4.21
3.51
Pre
Post

Chart 9


Degree of COPD vs BODE INDEX
Mean value
0
1
2
3
4
5
6
7
8
1.729
4.297
7.615
Mild
Moderate
Severe

DISCUSSION

COPD(Chronic obstructive pulmonary disease) is disorder which leads to significant mortality and morbidity. BODE index is a multidimensional grading system which predicts mortality better than FEV1. This multistage scoring system which includes an assessment of symptoms, nutritional state, and exercise capacity along with the spirometric measure of airflow (FEV_1) can provide useful prognostic information in patients with COPD.

Men are much more likely to be diagnosed with COPD then women, though the prevalence in women is on a steady raise [11].Even in our study males had a greater preponderance with 77% of them having COPD.In our study we found out that the prevalence of the disease increased with age more than 40 , though statistically it was not significant ; The results are similar to a study conducted by N.S. Zhong, P.X. Ran in China. Every 1 in 10 patients over the age of 40 years had COPD.

BODE INDEX & SEVERITY OF PULMONARY HYPERTENSION

10 - 30 % of patients with COPD develop pulmonary hypertension[52] ; Out of the 100 patients 57 developed pulmonary hypertension ; 43 did not develop pulmonary hypertension ;those who did not develop PHT had a mean BODE score of 2.0233. 6 patients had severe pulmonary hypertension(Mean BODE SCORE 8.1) ; 16 had moderate PHT,(mean BODE SCORE 7.120)and 35 had mild PHT ; according to our study the association between severity of pulmonary hypertension and high BODE score was statistically significant as shown by the p value < .001. Pulmonary HTN is caused due to hypoxic vasoconstriction, increase in lung volume,acidosis and secondary polycythemia.

COPD SEVERITY AND BODE SCORE

Total of 37 patients each were found in the mild and moderate COPD group;26 patients were found to have severe COPD. The mild and moderate group had a mean BODE score of 1.72 and 4.29 respectively.The severe COPD group had a mean BODE score of 7.6154.This was found to be statistically significant $p<0.001$

BODE SCORE AND NO. OF READMISSIONS

According to studies from Kian-Chung etal has proven that BODE scores correlates well with severity in terms of hospitalization and mortality. In a developing country where the health care resources are sparce BODE scoring system may be very helpful in health-care resource allocation and in guiding therapy for individual patients in the future.

Some studies showed a single BODE index assessment is enough to predict survival and hospital readmissions over 3 years in patients with chronic obstructive pulmonary disease (COPD). According to a study done by David Hui, a change in BODE index score of more than one point between baseline and 6 month assessment was marginally predictive of mortality, but serial changes in BODE index between the other time-points were not predictive of mortality.However, serial increases in BODE index of at least one point at 6, 12 and 24 months, were predictive of earlier readmissions to hospital. A single measurement of BODE index could predict mortality and readmissions over time. Ong et al, 2005[53] who found hospitalization and mortality in COPD patients higher with low 6m walk test. Also Celli et al, 2004(4) found that risk of death in

COPD patients was more with low 6min walk score.

In a study done by Adel Khattab, Khaled Wagih, Ahmed Mohamed by using BODE index as a predictor of risk of hospitalization in COPD patients, the results were statistically highly significant, indicated that risk of hospitalization increases by increasing BODE score. In our study we found that. 8 patients got admitted twice had a mean BODE score of 7.3750. 9 patients got admitted thrice had a mean bode score of 8.2222. This was statistically highly significant ($p < .001$).Hence as the BODE index increases the number of readmissions are more.

This was fully fit with Ong et al, 2005[53] study they used BODE index as predictor of hospitalization in COPD patients and compared it with FEV1classification of GOLD and found that BODE index was a better predictor of hospitalization than using FEV1 alone. As patients with higher BODE scores had higher rates of hospitalization.

DOWNSIZING OF BODE SCORE FOLLOWING INTERVENTION

A observational study done by C.G. COTE AND B.R. CELLI over one year in patients with COPD showed that, the response to Pulmonary Rehabitilation(PR) can be objectively measured using the BODE index and the change in BODE index provides information regarding ultimate survival.

Also, participation in a rehabilitation programme is associated with a decrease in hospitalizations. Rehabitilation has minimal effects on lung function but it improves dyspnea ,exercise capacity and health status.

According to Celli et tal [53] exercise capacity is a prognostic marker. The current authors defined one unit change in BODE as being clinically significant because it implies a change in any of its component of a magnitude large enough to influence clinical outcomes. This study also documented improvement in healthcare resources among these patients.

In our patients following interventions the mean BODE SCORE reduced from 4.21 to 3.51 which is a significant reduction in 6 months. The FEV1 levels came down indicating decrease in lung function despite therapy. The TRPG values increased mildly indicating increasing PHT. Though COPD is a progressive disease, an assessment of the post treatment improvement can be done and it has been demonstrated conclusively by the above studies. The BODE score, which is a composite marker of COPD severity, has been shown to decline significantly on treatment despite the contradictory evidence of the progression of the basic disease problem per se.

LIMITATIONS OF THE STUDY

1. This study includes local population and hence it is unlikely to represent the population all over the world.
2. The environmental factors thatplay a role in COPD differs from population to population, counrty to country which prevents us from generalizing the results to wider population.
3. The sample size was relatively small, to be able to give an unchallengeable statistically significant hypothesis.
4. The compliance of the patients is variable which could affect the study results especially the post intervention parameters.

SUMMARY AND CONCLUSIONS

In our study comprising hundred patients of COPD , conducted in government Stanley medical college ,we had compared BODE score with various parameters and analysed it statistically and got the following results ; Summarising

- BODE score was much better in predicting the morbidityand mortality associated with COPD than FEV1;
- Males were predominantly affected by COPD in our study ; this was in concordance with other similar studies ;
- The prevalence of COPD increased with age in our study and the association was statistically significant ;
- Maximum number of COPD patients occurred in the age group 50 – 60 years in our study ;
- BODE score correlated with the severity of COPD and PHT and this correlation was statistically significant in our study .

- Higher the BODE score, frequent the number of readmissions.
- BODE score is amenable to modification with appropriate medical intervention and thus can be used to assess therapeutic efficiency ;

CONCLUSIONS

1. BODE score correlates with severity of pulmonary hypertension and COPD.

2. BODE score can predict the number of readmissions in COPD patients;

3. BODE score can be inproved by adequate and timely therapeutic intervention and rehabilitative measures ;

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ABBREVIATIONS

ERS	-	European Respiratory Society
COPD	-	Chronic obstructive pulmonary disease
RV	-	Residual volume
PHT	-	Pulmonary hypertension
TLV	-	Total lung volume
FEV1	-	Forced expiratory volume in 1 sec
PI FEV1	-	Post intervention FEV1
IFN	-	Interferon
CD 8	-	Cluster of differentiation
MMP	-	Matrix metalloproteinases

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Correlation of BODE index with presence or absence of Pulmonary hypertension to predict further admissions Among patients with COPD

Principal Investigator : Dr.Anirudh J Shetty

Designation : PG in M.D(GM)

Department : Department of General Medicine
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 18.04.2011 at the Modernized Seminar Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate form the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

20/4/2011

MEMBER SECRETARY,
IEC, SMC, CHENNAI

PROFORMA

S.No	:	
Date	:	
Name	:	
Age	:	
Sex	:	F/M
Address	:	

PRESENTING COMPLANTS	:	
Cough with Expectoration	:	
Pedal edema	:	
Breathlessness	:	
Chest pain / Palpitation	:	
Past history	:	
DM / HT / IHD / CKD / COPD	:	
Personal history	:	
Family history	:	
Occupational history	:	
Examination	:	
Pulse	:	
BP	:	
JVP	:	

R.R :

HT :

WT :

BMI :

CVS :

RS :

Investigations :

CBC :

Sugar :

Urea :

Creatinine :

PFT Reversibility :

Resting SPO2 :

Xray Chest :

ECG :

ECHO :

Initial Admission :

Provisional Diagnosis :

	Pre Treatment	:	Post Treatment
BODE INDEX			
FEV1			
ECHO			

NAME	AGE	SEX	WT	HT	BMI	R.R	%FEV1	Sp O2	PHT	TRPG	BODE	COPD	ADM	P I BODE	P I % FEV1	P I TRPG
SUBBURAJ	42	M	50	1.6	19.5	21	51%	94%	moderate	48	6	severe	1	5	46%	51
UNNAMMAL	48	F	60	1.5	26.66	18	65%	99%	absent	30	0	mild	0	0	65%	30
PRABAKAR	52	M	55	1.45	26.15	16	55%	99%	mild	32	2	mild	0	2	52%	35
THANIKACHALAM	51	M	48	1.5	21.33	17	60%	99%	absent	28	2	mild	0	1	60%	28
AMUDAN	56	M	53	1.45	25.21	18	63%	98%	absent	26	4	moderate	0	3	63%	26
MUNIYAMMAL	49	F	58	1.39	30.05	16	54%	99%	Absent	24	3	moderate	0	2	54%	24
SHARADA	52	F	46	1.5	20.44	18	53%	98%	mild	38	5	moderate	0	4	52%	44
SUSHELA	49	F	48	1.48	21.9	17	57%	98%	mild	42	3	moderate	0	3	55%	42
PADMA	55	F	52	1.4	26.53	15	55%	98%	mild	33	3	moderate	0	3	53%	37
KANNNAN	50	M	55	1.55	22.87	16	44%	96%	moderate	55	7	severe	2	6	39%	58
SURAJ	49	M	49	1.54	20.66	14	59%	99%	mild	36	4	moderate	1	3	56%	36
RAJAN	51	M	50	1.5	22.22	22	60%	99%	mild	44	5	moderate	1	4	59%	49
KARTIKEYAN	57	M	49	1.52	21.2	17	54%	99%	mild	41	4	moderate	1	4	52%	44
SRIDHAR	58	M	56	1.4	28.57	14	53%	99%	absent	26	2	mild	0	2	53%	26
SUNDAR	62	M	60	1.58	24.03	14	34%	95%	moderate	60	8	severe	3	7	30%	64
SANTOSH	50	M	51	1.6	22.6	19	55%	99%	mild	41	5	moderate	1	4	54%	45
JAMES	40	M	49	1.39	25.36	16	53%	99%	mild	38	3	moderate	0	3	52%	43
SUBRAMANI	70	M	50	1.55	20.8	18	39%	97%	moderate	60	7	severe	0	6	34%	60
MANIKANTHAN	46	M	46	1.46	21.4	19	40%	99%	mild	33	8	severe	0	6	40%	38
GOPALAKRISHNAN	50	M	56	1.6	21.8	22	48%	99%	mild	42	5	moderate	1	4	45%	46
SUKUMAR	38	M	49	1.7	16.9	18	60%	97%	moderate	64	8	severe	0	7	55%	67
CHINNARAJ	61	M	59	1.5	26.22	17	63%	99%	absent	26	3	moderate	0	2	63%	26
DHARMAR	60	M	60	1.72	20.28	16	59%	99%	absent	25	3	moderate	0	3	59%	25
DEVAN	60	M	51	1.7	17.64	17	48%	99%	mild	36	6	severe	1	5	47%	36
RAMESH	42	M	47	1.5	20.8	18	55%	99%	absent	25	4	moderate	0	3	55%	25
PERUMAL	85	M	50	1.41	25.15	15	44%	99%	mild	39	5	moderate	1	5	43%	43
MURUGA	38	M	60	1.7	20.7	14	55%	99%	absent	30	3	moderate	0	3	55%	30
ELANGO	62	M	47	1.42	23.37	20	58%	99%	absent	27	4	moderate	0	3	58%	27
ASHWIN	42	M	44	1.5	19.55	16	50%	99%	mild	44	5	moderate	1	4	48%	48

NAVEEN	45	M	49	1.46	22.99	18	40%	96%	moderate	55	7	severe	2	6	35%	57
RAJENDRAN	38	M	67	1.5	25.33	21	30%	90%	severe	75	9	severe	3	7	24%	79
VENKATESH	53	M	54	1.62	20.59	19	58%	99%	absent	29	2	mild	0	2	58%	29
SHANTHAKUMAR	55	M	56	1.61	21.8	22	62%	99%	absent	22	2	mild	0	1	62%	22
JAYAPAL	50	M	56	1.7	19.3	15	60%	99%	absent	28	3	moderate	0	2	60%	28
CHELLAYA	60	M	46	1.48	21.4	17	45%	99%	mild	39	5	moderate	1	4	43%	43
SAGARAJ	47	M	60	1.54	25.6	19	55%	99%	mild	41	4	moderate	1	3	54%	44
ABDUL	65	M	56	1.5	24.88	20	52%	99%	absent	26	2	mild	0	2	52%	26
JOHN	67	M	54	1.6	21.09	21	38%	97%	moderate	60	7	severe	3	6	34%	64
TIRUPATHI	30	M	56	1.62	21.34	22	63%	99%	absent	27	1	mild	0	1	63%	27
SHAKTIVEL	35	M	47	1.5	20.88	14	61%	99%	absent	23	2	mild	0	2	61%	23
WILLIAMSON	45	M	45	1.4	22.95	19	58%	99%	absent	19	1	mild	0	1	58%	19
BALAJI	45	M	61	1.51	26.75	17	42%	99%	mild	35	5	moderate	1	4	41%	39
LOGANATHAN	39	M	50	1.6	19.5	15	52%	98%	mild	43	6	severe	1	5	51%	47
BHAVANI	45	F	60	1.5	26.66	20	58%	97%	absent	27	2	mild	0	2	58%	27
BHUVANESHWARI	38	F	55	1.45	26.15	19	61%	99%	absent	26	2	mild	0	1	61%	26
SHANMUGAN	40	M	48	1.5	21.33	15	40%	95%	moderate	66	8	severe	3	7	36%	66
MALLIKA	60	F	53	1.45	25.21	18	60%	99%	absent	26	1	mild	0	1	60%	26
SHANKAR	50	M	58	1.7	20.06	22	43%	97%	moderate	63	8	severe	3	7	38%	67
SHANTHI	52	F	46	1.5	20.44	21	26%	92%	severe	75	9	severe	4	7	20%	78
SHIVAMOORTHY	60	M	48	1.35	26.34	16	64%	99%	absent	26	2	mild	0	2	64%	26
VENKATACHALAM	58	M	52	1.4	26.53	18	62%	99%	absent	29	2	mild	0	2	62%	29
GOVINDAMMAL	56	F	55	1.61	21.2	19	34%	95%	moderate	35	9	severe	2	7	29%	39
GAURI	72	F	49	1.58	19.64	22	24%	90%	severe	75	8	severe	3	7	18%	79
MUNUSWAMY	69	M	50	1.5	22.22	20	29%	94%	moderate	48	6	severe	2	6	25%	52
SUBALAKSHMI	46	F	61	1.71	21.4	17	46%	99%	mild	36	5	moderate	1	5	46%	40
SETHURAMAN	45	M	56	1.4	28.57	14	55%	99%	absent	20	2	mild	0	2	55%	20
CHINAMMAL	40	F	60	1.51	25.34	14	61%	98%	absent	25	2	mild	0	1	61%	25
MANIMARAN	55	M	51	1.6	19.92	21	40%	99%	mild	33	8	severe	1	6	40%	37
BALAMANI	68	F	49	1.39	25.36	18	64%	99%	absent	28	1	mild	0	1	64%	28

LINGAM	66	M	50	1.3	29.58	16	66%	99%	absent	26	1	mild	0	1	66%	26
RANI	80	F	46	1.32	26.4	17	45%	99%	mild	49	5	moderate	1	4	40%	49
FATHIMA	60	F	56	1.7	19.3	18	38%	99%	mild	44	3	moderate	0	2	38%	47
JAYALAKSHMI	46	F	49	1.61	18.9	16	26%	95%	moderate	60	8	severe	2	7	21%	64
SARALA	57	F	59	1.5	26.22	18	65%	99%	mild	56	2	mild	1	2	60%	56
RAJESH	50	M	60	1.4	30.61	17	63%	98%	absent	20	1	mild	0	1	63%	20
KIRBAKAVAN	45	M	56	1.45	26.64	15	57%	99%	absent	27	2	mild	0	2	57%	27
MURUGANDAM	35	M	54	1.6	21.09	16	50%	99%	mild	38	5	moderate	1	4	49%	42
RANKUMAR	40	M	56	1.33	31.8	14	65%	98%	absent	28	2	mild	0	2	65%	28
KARTHIK	60	M	47	1.5	20.88	22	40%	97%	moderate	66	5	moderate	1	4	35%	70
SHANMUGAN	65	M	45	1.4	22.95	17	39%	98%	mild	39	8	severe	1	8	37%	44
KRISHNAN	46	M	61	1.51	26.75	14	45%	98%	mild	43	5	moderate	1	5	43%	43
SIDDIQUE	62	M	50	1.6	19.5	14	30%	97%	moderate	69	8	severe	2	7	26%	71
LOGANATHAN	52	M	60	1.5	26.66	19	61%	99%	absent	24	2	mild	0	2	61%	24
SHIVA	60	M	55	1.45	26.15	22	49%	99%	mild	43	5	moderate	1	3	47%	46
RAMU	50	M	58	1.44	27.97	17	63%	98%	absent	23	2	mild	0	2	63%	23
SALAI	56	M	53	1.45	25.21	19	60%	99%	absent	25	2	mild	0	1	60%	25
SALIM	47	M	58	1.5	25.77	20	55%	98%	absent	20	1	mild	0	1	55%	20
LOGANAYAGI	67	M	49	1.53	20.9	16	32%	96%	moderate	59	7	severe	1	5	27%	59
MANJULA	40	F	59	1.51	26.22	17	54%	98%	absent	22	2	mild	0	2	54%	22
KANIKA	34	F	60	1.4	30.61	19	60%	99%	absent	21	2	mild	0	1	60%	21
JAYAVELA	62	M	50	1.55	20.8	20	39%	96%	moderate	65	5	moderate	2	4	34%	65
SRIRAM	70	M	58	1.63	21.83	14	27%	99%	mild	38	6	severe	1	4	27%	40
KARPAGAM	65	F	56	1.7	19.37	20	29%	89%	severe	74	9	severe	3	8	23%	77
VADIVEL	57	F	59	1.58	23.63	21	45%	98%	mild	33	5	moderate	1	4	44%	33
MARY	48	F	49	1.6	19.14	19	39%	99%	mild	39	5	moderate	1	5	36%	42
DINAKAR	67	M	70	1.55	20.8	22	32%	93%	severe	73	9	severe	2	7	23%	75
SAMPATHAN	50	M	46	1.46	21.4	18	65%	99%	absent	22	2	mild	0	1	65%	22
PERUMAL	49	M	56	1.62	21.34	17	55%	99%	absent	27	2	mild	0	1	55%	27
KRISHNAMOORTHY	60	M	49	1.7	16.9	16	44%	97%	mild	41	5	moderate	0	4	44%	45

VELAUDHAM	55	M	49	1.46	22.99	17	60%	99%	absent	18	2	mild	0	1	60%	18
SABARIMUTHU	46	M	57	1.5	25.33	15	61%	99%	absent	19	2	mild	0	1	61%	19
MURUGAN	58	M	54	1.62	20.59	16	40%	99%	mild	40	4	moderate	1	3	39%	44
GUNASEKARAN	46	M	56	1.53	24.3	14	53%	99%	absent	28	2	mild	0	1	53%	28
MUNIANDI	52	M	50	1.6	19.5	22	39%	99%	mild	44	5	moderate	1	4	39%	44
ELUMALAI	49	M	60	1.5	26.66	17	65%	98%	absent	27	2	mild	0	1	65%	27
ELANGOVAN	51	M	55	1.45	26.15	14	62%	99%	absent	19	1	mild	0	1	62%	19
CHINAKUTI	54	M	48	1.5	21.33	20	30%	99%	mild	32	5	moderate	1	4	29%	35
EGAMBARAM	43	M	53	1.45	25.21	18	50%	99%	absent	30	2	mild	0	2	50%	30
VENKATIAH	48	M	66	1.7	20.06	19	22%	92%	severe	76	8	severe	3	8	15%	76